

Amendments to the Claims

The following listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) An implantable active agent delivery device for providing an active agent to a subject, the delivery device comprising:

(a) a reservoir having a volume of active agent;

[[ (a) ] (b) a biomaterial comprising:

(i) a core ~~having a volume of active agent,~~ wherein the core is in fluid communication with the reservoir,

(ii) a front surface, and

(iii) a back surface,

wherein the front surface of the biomaterial is adapted to be held

substantially adjacent to vascular tissue within the subject,

wherein the biomaterial is capable of administering the active agent or of

providing a metabolic or immunologic function to the subject;

[[ (b) ] (c) an external selectively permeable jacket surrounding the core, the jacket comprising a biocompatible membrane having a molecular weight cutoff permitting passage of molecules of the active agent to and from the core through the jacket to adjacent vascular tissue within the subject; and

[[ (c) ] (d) a tether coupled with the biomaterial, wherein the tether is configured to anchor the biomaterial at an implantation site, wherein the tether comprises a tube configured to replenish the ~~core~~ reservoir.

2. (canceled)
3. (previously presented) The device of claim 1, wherein the tether is adapted to hold the biomaterial substantially adjacent to vascular tissue.
4. (previously presented) The device of claim 1, wherein the tether material is bioabsorbable.
5. (canceled)
6. (previously presented) The device of claim 1 wherein the device further comprises a radio-opaque marker material.
7. (original) The device of claim 3 wherein the device is adapted for delivery of active agent to the peritoneum.
8. (original) The device of claim 3 wherein the device is adapted for delivery of active agent to the omentum.
9. (original) The device of claim 7 or 8 wherein the delivery device is adapted for delivery through a cannula.
10. (canceled)

11. (previously presented) The device of claim 1, wherein the active agent is stable in the presence of elevated temperature or organic solvents.

12. (original) The device of claim 1, 7 or 8 wherein the active agent is selected from the group consisting of antibodies, enzymes, trophic factors, growth factors, hormones and biological response modifiers.

13. (original) The device of claim 1, 7 or 8 wherein the active agent is an analgesic or pain-reducing substance.

14. (original) The device of claim 12, wherein the active agent is a peptide or protein.

15. (original) The device of claim 14 wherein the active agent is a cytokine or lymphokine.

16. (previously presented) The device of claim 1, wherein the active agent is an immunogen.

17. (previously presented) The device of claim 1, wherein the active agent is prophylactic for use as a vaccine.

18. (previously presented) The device of claim 1, wherein the active agent comprises an antigen and an adjuvant.

19. (previously presented) The device of claim 1, wherein the biomaterial further comprises one or more delivery enhancing agents selected from the group consisting of polyethylene oxide (PEO), heparin, albumin, tissue growth factors, angiogenic growth factors, surfactants, anti-oxidants, anti-inflammatory agents, and anti-rejection medications.

20. (previously presented) The device of claim 19, wherein the angiogenic growth factor is selected from the group consisting of basic fibroblast growth factor, acidic fibroblast growth factor, vascular endothelial growth factor, platelet derived endothelial cell growth factor bb, angiopoietin-1, transforming growth factor beta, transforming growth factor alpha, hepatocyte growth factor, tumor necrosis factor-alpha, angiogenin, interleukin-8, hypoxia inducible factor-i, angiotensin-converting enzyme inhibitor quinaprilat, angiotropin, thrombospondin, lactic acid, insulin, and growth hormone.

21. (previously presented) The device of claim 19, wherein the anti-inflammatory agent is selected from the group consisting of cortisone and ACTH, dexamethasone, cortisol, interleukin-1 and its receptor antagonists, and antibodies to TGF-beta, to interleukin-1 (IL-1), and to interferon-gamma.

22. (previously presented) The device of claim 1, wherein the device is adapted for delivery of active agent at a dose rate from about 0.001 to about 200 micrograms/hr.

23. (previously presented) The device of claim 1, wherein the device is adapted for delivery of active agent at a volume rate of from about 0.01 microliters/day to about 2 ml/day.

24. (previously presented) The device of claim 1, where the back surface of the biomaterial further comprises a substantially resilient substrate material capable of substantially maintaining the shape of the biomaterial.

25. through 27. (canceled)

28. (currently amended) The device of claim [[25]] 1, ~~further comprising a reservoir, wherein the reservoir contains active agent and is adapted to delivering~~ deliver the active agent to the front surface for delivery to the tissue.

29. (withdrawn – currently amended) The device of claim [[25]] 1, wherein the device further comprises a penetration enhancer.

30. (withdrawn) The device of claim 29 wherein the penetration enhancer is selected from the group consisting of cell-envelope disordering compounds, solvents and mixtures thereof.

31. (canceled)

32. (previously presented) The device of claim 1, wherein the molecular weight cutoff of the membrane is between about 50 - 2000 kD.

33. (previously presented) The device of claim 1 wherein the molecular weight cutoff of the membrane is above about 100 kD.

34. (previously presented) The device of claim 1 wherein the core comprises a biocompatible matrix formed from a hydrogel.

35. (original) The device of claim 34, where the hydrogel is impregnated with pharmaceuticals.

36. (previously presented) The device of claim 1 wherein the jacket is selected from the group consisting of polyacrylonitrile-polyvinylchloride, polyacrylonitrile, polymethylmethacrylate, polyvinylidifluoride, polyolefins, polysulfones and celluloses.

37. (original) The device of claim 36 wherein the jacket further comprises a hydrophilic or hydrophobic additive.

38. (previously presented) The device of claim 1, where the biomaterial is a tissue matrix structure.

39. (original) The device of claim 38, where the tissue matrix structure includes mammalian cells.

40. (original) The device of claim 39 wherein the cells are allogeneic or syngeneic upon implantation.

41. (original) The device of claim 39 wherein the cells are selected from the group consisting of insulin-producing cells, adrenal chromaffin cells, antibody-secreting cells, fibroblasts, astrocytes, Beta cell lines, and Chinese hamster ovary cells.

42. (original) The device of claim 39 wherein the cells are insulin-producing cells.

43. (original) The device of claim 39 wherein the cells secrete antibodies.

44. (original) The device of claim 39 wherein all of the cells are disposed at a distance no greater than about 800  $\mu\text{m}$  from the front face of the device.

45. (original) The device of claim 39 wherein the delivery device further comprises a core comprising a volume in excess of 1  $\mu\text{l}$  and at least about  $10^4$  living cells dispersed in a biocompatible hydrogel matrix, the cells being capable of secreting a active agent or of providing a metabolic or immunologic function.

46. (currently amended) The device of claim 39, ~~further comprising a reservoir,~~  
wherein the reservoir contains nutrient-rich material and is adapted to delivering the nutrient-rich  
material to the cells.

47. (original) The device of claim 39 wherein the cells are aggregated into a  
diffusional aggregate form adapted for increased packing per unit volume.

48. through 60. (canceled)